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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,813	03/06/2002	Kelly Huang	JBP-581	8501

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/091,813	HUANG ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *11-17 and 19-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-17 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/21/2006 has been entered.

2. Claims 11-17 and 19-22 are pending.

3. Claim 18 was cancelled in the reply filed on 08/21/2006.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-22 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons as set forth in the Office action mailed on 04/17/2006. This a new matter rejection.

Applicant's arguments filed on 08/21/2006 have been fully considered, but are not found pursuasive. Applicant argues that the specification is replete with discussions of a method of measuring the subclinical or clinical inflammation or irritation of mammalian skin due to exposure of topical skin care products by measuring eicosanoid. For example, on page 5, lines 9-26. Applicant's point to Example 3 to see a measure of the levels of eicosanoid after exposure to a topical skin care product comprising anionic surfactant ammonium laureth sulfate. Applicants stresses that newly added claim limitations can be supported in the specification through express, implicit or inherent disclosure.

While Applicant does having written support for measuring eicosanoid levels in topical skin care products that have anionic surfactants in them in addition to external aggression, there is no written support in the specification or claims as originally filed for measuring eicosanoid levels in response to only applying a topical skin care product that generically has an anionic surfactant in it. The ammonium laureth sulfate of Example 3 is one of fifteen ingredients in the topical skin care product. Therefore, any level of irritation or inflammation resulting from the application of the topical skin care product of Example 3 could not be attributed to the ammonium laureth sulfate with any certainty.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 11-15 and 17-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller-Decker et al., (reference AH on the IDS submitted 3-6-02) in view of Perkins et al., 1997, (reference AG submitted in the IDS received 3-6-02) for the same reasons as set forth in the Office Action mailed on 04/20/2005.

Applicants arguments filed on 08/21/2006 have been fully considered, but are not found persuasive. Applicants argue that the non-invasive Sebutape of Perkins et al. does not cure the deficiency of the invasive method of Mueller-Decker et al. because there is no teaching or suggestion in the reference that Sebutape could be used to determine the level of eicosanoid, nor does Perkins mention eicosanoids

However it is the Examiner's position that Perkins et al., specifically teaches a non-invasive method for assessing human skin irritation using Sebutape™, an adhesive coated microporous plastic film that detects IL-1 α due to inflammatio/irritation even in the absence of visible clinical irritation. Perkins et al., further teaches that said tape can be easily applied in a clinical setting whether on infants, adults or geriatric adults.

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to screen for skin irritation by detecting PGE_2 and IL-1 α, as taught by Mueller-Decker et al., but substitute the use of Sebutape™, as taught by Perkins et al., because Sebutape™ is able to detect molecular mediators of skin irritation without being invasive or requiring visible clinical irritation.

9. Claims 11, 16 and 22 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller-Decker et al., in view of Perkins et al., as applied to claim 11 above, and further in view of Reilly et al, all of record for the same reasons as set forth in the Office Action mailed on 04/20/2005.

Applicant's arguments filed on 08/21/2006 have been fully considered, but are not found persuasisve. Applicant's argue that Reilly et al. does not cure the deficiency of Mueller-Decker et al. or Perkins et al.

However, Mueller-Decker et al., does teach normalizing PGE_2 levels to the level of fat and it also teaches measuring PGE_2 by GC/MS. Reilly et al., specifically teaches normalizing PGE_2 levels to the level of protein and measuring PGE_2 levels by EIA.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to be motivated substitute one known method of measuring PGE_2 by EIA rather than GC/MS and normalizing PGE_2 with one known method, lipid levels for another known method, protein levels.

10. In view of the amendments to the claims filed on 08/21/2006, the following new grounds of rejection are set forth below.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 11-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

Applicant has amended the claims by the insertion of measuring a baseline level of eicosanoid and at least one cytokine after exposing skin to a topical skin care product comprising anionic surfactant in order to measure inflammation. Applicant has written support for measuring eicosanoid levels in topical skin care products that have anionic surfactants in them in addition to external aggression, but there is no written support in the specification or claims as originally filed for measuring eicosanoid levels in response to only applying a topical skin care product that generically has an anionic surfactant in it. In addition, there is no written support in the specification or claims as originally filed for measuring eicosanoid and at least one cytokine level in response to only applying a topical skin care product that generically has an anionic surfactant in it.

6. Claims 11-22 are rejected under 35 U.S.C. 112, first paragraph, first paragraph, because the specification, while being enabling for a method of measuring IL-1 α after external aggression or a topical skin care product with anionic surfactant; and PGE_2 in response to external aggression and topical skin care products, external aggression alone, topical skin care products alone and in response to water does not reasonably provide enablement for a method for measuring sub-clinical or clinical inflammation or irritation of mammalian skin from exposure of said skin to a topical skin care product, exposure to an external aggression or combinations thereof, said method comprising the steps of: (a) collecting secretions from the surface of said skin using a non-invasive collection procedure comprising a non-invasive collection device; (b) **measuring a baseline level of eicosanoid and a baseline level of at least one cytokine in the secretions collected from the surface of said skin**; (c) exposing said

skin to a topical skin care product, to an external aggression or combinations thereof; (d) collecting secretions from the surface of said skin using a non-invasive collection device after step (c); (e) measuring the level of eicosanoid and the level of at least one cytokin in the secretions collected from the surface of said skin after step (c); and (f) comparing the level of eicosanoid determined in step (e) with the level of eicosancid determined in step (b); wherein said non-invasive collection procedure comprises using a non-invasive collection device, said noninvasive collection device selected from the group consisting of an uncoated non-porous plastic film, an uncoated microporous plastic film, an adhesive-coated nonporous plastic film, an adhesive-coated microporous plastic film, a woven fibrous web, a non-woven fibrous web, a natural sponge, a synthetic sponge and a plastic foam of claim 12; wherein said non-invasive collection device comprises an adhesive-coated microporous plastic film of claim 13; wherein said eicosanoid is prostaglandin of claim 14; wherein said prostaglandin is prostaglandin PGE_2 of claim 15; wherein the level of eicosanoid is measured using at least one immunoassay technique selected from the group consisting of RIA, EIA and ELISA of claim 16; wherein the level of eicosanoid is measured using analytical techniques selected from the group consisting of GC/MS, HPLC, and TLC of claim 17; **wherein said cytokine is IL-1 α** of claim 19; **wherein said cytokine is IL-1 α and said eicosanoid is prostaglandin PGE_2** of claim 20; wherein step (d) is performed about 24 hours after step (c) of claim 21; the method further comprising the step of: measuring the level of protein in the skin secretions and normalizing the level of eicosanoid to the level of protein of claim 22.

The specification discloses a method of 1.) measuring IL-1 α after external aggression (see Example 6) or after a topical skin care product with anionic surfactant (see Example 2) and 2.) measuring PGE_2 in response to external aggression and topical skin care products (see Example 5), external aggression alone (see Example 4), topical skin care products alone (see Example 3) and water (see Example 1). However, applicant is not enabled for measuring sub-clinical or clinical inflammation resulting from the skin IL-1 α and PGE_2 response to a topical skin care product with anionic surfactant.

The specification, discloses on page 20 that the amount of IL-1 α "is expected to increase as the level of the anionic surfactant, SLS, increases. While this is observed at low SLS levels, this is not seen at the highest concentration of SLS tested in the study, raising a potential issue as to the robustness of the method. While wishing not to be bound by theory, it is thought that high concentrations of anionic surfactants, such as SLS, may interact with proteins, such as IL-1.alpha., causing denaturation of the proteins. This process would affect the immunoassays, and could result in the lower apparent levels of IL-1.alpha. that are observed in this experiment at the highest SLS concentration. When analyzing for levels of IL-1.alpha. using immunoassays, the SLS may change the conformation of the protein, rendering it unrecognizable by the antibody used in the assay. Thus, using the levels of IL-1.alpha. to assess the degree of irritation is limited due to these potential surfactant-protein interactions." Therefore, Applicant is not enabled for measuring sub-clinical or clinical inflammation or irritation of mammalian skin from exposure of the skin to a topical skin care product comprising anionic surfactant by measuring the baseline level of IL-1 α and PGE_2 because IL-1 α is denatured by the anionic surfactant at higher concentrations and cannot be accurately measured.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 11-15 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller-Decker et al., (reference AH, IDS 03/06/2002) in view of Perkins et al., 1997, (Reference AG, IDS 03/06/2002) and newly cited European Patent 0497399 A1 (EP 399' patent) (Reference AW, IDS 03/06/2002).

Mueller-Decker et al., teaches it is necessary to assess skin irritation to protect humans from the hazards of topical exposure of environmental, industrial and consumer chemicals. The reference also discloses an invasive method measuring PGE_2 levels in skin blister fluid to determine skin irritation in response to topical application of SLS in aqua bidest; wherein said PGE_2 levels are measured by GC/MS; wherein said levels are measured against a control; wherein IL-1-α levels measured; and wherein said measuring is performed 24 hours after the applying the SLS.

The claimed invention differs from the prior art by the recitation of using a non-invasive adhesive coated microporous plastic film to collect the skin samples as secretions to detect skin irritation.

Perkins et al., specifically teaches the use of Sebutape™, an adhesive coated microporous plastic film product for non-invasive assessment of human skin irritation Sebutape is used to detect IL-I α, even in the absence of visible clinical irritation. The reference also teaches that Sebutape can be easily applied in a clinical setting on infants, adults or geriatric adults.

The EP 399' patent teaches a process for evaluating skin irritancy. On the last paragraph of page 4, the reference teaches that PGE_2 is detected in intact mouse and human skin treated with sodium dodecyl sulfate using a non-invasive sampling technique. Though the reference in silent as to the non-invasive technique, the samples are taken from intact skin. The data indicates that " PGE_2 may be an excellent in vitro biomarker" of irritant induced inflammation that has "direct relevance to human clinical results".

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to screen for skin irritation by detecting IL-1 α (as taught by Perkins et al.) and PGE_2 (as taught by the EP 399' patent and Mueller-Decker et al.), but to substitute the use of Sebutape™ (as taught by Perkins et al.) because Sebutape™ is able to detect molecular mediators of skin irritation without being invasive and being able to detect said compounds prior to visible clinical irritation and because "it can be easily applied in a clinical setting whether on infants, adults or geriatric adults."

Applicant argues that Perkins et al. does not have any "teaching or suggestion that Sebutape could be used to determine the level of eicosanoid."

Because Sebutape functions by "adsorption of molecular mediators" after placing the tape on the skin to "extract" the molecules from the skin sites, one would have an high expectation of success in sampling many types of molecules. One of ordinary skill in the art would be motivated to extract PGE_2 along with the already successfully extracted IL-1 α from the skin since the physical mechanism of extraction from the skin onto the tape is the same. One would also be motivated to use Sebutape to sample PGE_2 from the skin because of it is non-invasive and easy to use in a clinical setting and because PGE_2 is an excellent in vitro biomarker irritant induced inflammation with direct relevance to human clinical results (as taught by the EP 399' patent).

10. Claims 11, 16 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller-Decker et al., in view of Perkins et al. and newly cited European Patent 0497399 A1 (EP 399' patent) (Reference AW, IDS 03/06/2002) as applied to claim 11 above, and further in view of Reilly et al, all of record.

Mueller Decker et al., and Perkins et al., have discussed *supra*. Mueller-Decker et al., further teaches normalizing PGE_2 levels to the level of fat and it also teaches measuring PGE_2 by GC/MS.

The claimed invention differs from the prior art by the recitation of normalizing PGE_2 levels by protein levels and by measuring PGE_2 by EIA.

However, Reilly et al., specifically teaches normalizing PGE_2 levels to the level of protein and measuring PGE_2 levels by EIA.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to be motivated substitute one known method of measuring PGE_2 by EIA rather than GC/MS and normalizing PGE_2 with one known method, lipid levels for another known method, protein levels. One of ordinary skill in the art would substitute the clinically effective Sebutape of Perkins et al. for the invasive

collection method of Mueller-Decker et al. to measure skin irritation in response to topical application of SLS in aqua bidest; wherein said PGE_2 levels are measured by GC/MS; wherein said levels are measured against a control; wherein IL-1-α levels measured; and wherein said measuring is performed 24 hours after the applying the SLS. It would also be obvious to further measure PGE_2 by EIA and to normalize PGE_2 levels by comparing them to protein levels as taught by Reilly et al.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 8, 2007

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PATENT EXAMINER

1/5/07